MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Individual Safety Report

3133426-7-00-01

15/93

McNEIL CONSUMI
FORT WASHINGTON, PA 19034

Page ____ of ____

FDA use only

A. Patient information

1. Patient Identifier	2. Age at time of event:	3. Sex	4. Weight
unknown In confidence	11 mo or Date of birth:	( )female (X)male	unk lbs or kgs

B. Adverse event or product problem

1. X Adverse event and/or Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

( ) death (mo/day/yr)
( ) life-threatening
(x) hospitalization - initial or prolonged
( ) disability
( ) congenital anomaly
( ) required intervention to prevent permanent impairment/damage
(x) other: recovered

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)
unknown	09/09/98

5. Describe event or problem

Literature report(J Toxicol Clin Toxicol 1998; 36(5):443) of fulminant HEPATIC FAILURE in an 11 mon. old male from the 1998 NACCT Abstracts.Case report indicates a previously healthy male presented unresponsive w/profound HYPOGLYCEMIA after a 3 day illness of FEVER, VOMITING, STOMATITIS, & decreased intake (ANOREXIA). Recent meds include acetamino-) as suspension, suppositories & as part of a multi- ptom cold remedy.In ER, pt treated w/IV dextrose, evaluated for presumed sepsis & started on antibiotics.On morning after Adm., pt became unresponsive & required intubation. Pt fulfilled the criteria for stage IV hepatic encephalopathy & was treated w/supportive therapy including a double volume exchange transfusion.Pt placed on liver transplant list.Pt rec'd 72h course of NAC.Pt progressed to a full recovery & was d/c 10 days after Adm.After discharge, metabolic studies revealed the etiology to be Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency.

6. Relevant tests/laboratory data, including dates

On morning after Adm.:normal blood glucose,AST,ALT greater than 10,000 IU/L,LDH= 6180U/L,NH3-190mcmol N/L,PT greater than 50sec,PTT=55sec,bilirubin=9.2/6.1mg/dL;acetaminophen level= 10mg/L(Last known dose of acetaminophen (See Sect B7)

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

Unknown; (Sect B6 cont.): was prior to admission, more than 24 hours previously).

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 acetaminophen suspension
#2 acetaminophen suppository

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration) from/to (or best estimate)
#1 unknown dose, po	#1 unknown
#2 unknown dose, rectally	#2 unknown

4. Diagnosis for use (indication)

#1 unknown
#2 unknown

5. Event abated after use stopped or dose reduced

#1 (X) Yes ( ) No ( ) N/A
#2 ( ) Yes ( ) No (X) N/A

6. Lot # (if known)	7. Exp. date (if known)
#1 Unknown	#1 Unknown
#2 unknown	#2 unknown

8. Event reappeared after reintroduction

#1 ( ) Yes ( ) No (X) N/A
#2 ( ) Yes ( ) No (X) N/A

9. NDC # - for product problems only (if known)

- -

10. Concomitant medical products and therapy dates (exclude treatment of event)

Sect C1 cont.: #3 multi-symptom cold remedy, unknown dose, po

G. All manufacturers

1. Contact office - name/address (& mfring site for devices)

McNeil Consumer Products Company
Medical Affairs
7050 Camp Hill Road
Ft. Washington, PA 19034

2. Phone number: 215-233-7820

3. Report source (check all that apply)

( ) foreign
( ) study
(x) literature
( ) consumer
(x) health professional
( ) user facility
( ) company representative
( ) distributor
( ) other:

4. Date received by manufacturer (mo/day/yr): 09/09/98

6. (A) NDA # 19-872
IND #
PLA #
pre-1938 ( ) Yes
OTC product (X) Yes

6. If IND, protocol #

7. Type of report (check all that apply)

( ) 5-day (X) 15-day
( ) 10-day ( ) periodic
(X) Initial ( ) follow-up #

8. Adverse event term(s)

HYPOGLYCEMIA
FEVER
VOMITING
STOMATITIS
ANOREXIA
LIVER FAILURE

9. Mfr. report number: 1032389A

E. Initial reporter

1. Name, address & phone #

[redacted]

SEP 22 1999

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
(X) Yes ( ) No	health prof.	( ) Yes ( ) No (X) Unk

FDA

Facsimile Form 3600A

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

34 NEPHROTOXICITY FOLLOWING DERMAL ABSORPTION OF BROMATE.

Gorman SE, Warshaw BL, Garrettson LK. *Georgia Poison Center & Emory University, Atlanta, GA*

Background: Bromate induced nephrotoxicity has followed ingestion. Such injury has not been reported following dermal absorption. Case Report: ProLine SuperCurly Neutralizer was applied twice to the hair of a healthy 9-year-old girl with normal intelligence. 30 minutes after application, which induced a severe burning sensation on the scalp, she vomited. 2 hours later, loose stools, along with the vomiting, led to hospitalization for acute gastroenteritis. BUN was 35mg/dL and creatinine (C_R) 1.9mg/dL on admission. The 4th day after exposure, BUN/C_R were 73mg/dL/7.0mg/dL. She was transferred to a tertiary center where the association with bromate was entertained. The girl denied any ingestion of the product. Her mother, present during the application, reported no incident where the products would have entered her mouth. The second application was triggered by severe stinging during the first, yet, it also caused stinging. The dermal route of absorption was the only route identified. A serum bromide was 11mg/dL. Her scalp showed diffuse thin brown desquamation; however, there was no active dermatitis at that time. The hair was brittle. On day 5, peritoneal dialysis was started and continued 6 days. BUN/C_R peaked at 95mg/dL/11.7mg/dL on day 7. On day 5, AST was 47U/L; CPK 375U/L; and LDH 832U/L. Total parenteral nutrition was needed because of emesis and anorexia which waned by day 12. She was discharged on day 14 eating normally and on iron for a drop in hemoglobin from 12.5 to 8.5 g/dL. Audiometry on discharge revealed normal hearing. Results: No oral exposure was identified. The scalp was injured more than expected from routine use. This would occur if the concentration of the product were too high. Bromide in the serum showed absorption. Injury to the kidney from bromate is supported. The manufacturers, notified about the case, are reviewing their marketing of this product. Conclusions: Dermal absorption of bromate in toxic amounts can occur. The authors think bromate should be removed from the cosmetics market.

35 ACUTE ALLERGIC REACTION TO HAIR WAVING AGENTS.

Fogel J, Díaz JE. *Emergency Medicine Department. Cooper Hospital/University Medical Center-RWJ, Camden, NJ*

Background: Historically, cosmetic products when used according to labeling information present a limited health threat. Commonly reported toxicity is of a contact dermatosis. Most Hair Waving Agents are classified as caustic agents with a potential for serious chemical burns when misused. Acute systemic symptoms are unusual. We report two cases of an "*Immunologic Contact Urticaria Syndrome*". Case Series: 1) A previously healthy, 31 year-old female was evaluated 30min after a mixture of African Pride® Relaxer and Activator was applied to her scalp hair. She developed pruritus that started with scalp burning. She stated that her lips were swollen. Her vital signs were BP 139/80; HR 125 (narrow ST); RR 24; T 97.4; POx 95%^{RA}. Her airway, breathing, and circulatory assessment were normal. Facial flushing and urticaria was noted. Treatment consisted of decontamination, antihistamines and corticosteroid. 2) A 26 year-old female with history of asthma fainted shortly after applying AAA Bond® to her scalp hair. First, she experienced scalp burning and itching. Subsequently, she became nauseous, light-headed, diaphoretic, short-of-breath, and complained of substernal and stomach burning. She became unconscious and awoke without confusion. Her vital signs were BP 86/60; HR 124 (narrow ST); RR 24; POx 97%^{RA}. Her airway, and breathing assessment were normal. She had hyperemic conjunctivas. Significant lacrimation was noted. Urine drug screen was negative. Treatment consisted of decontamination, a fluid challenge, antihistamines, and corticosteroid. Conclusions: Due to allergen induced sensitization, most contact cutaneous disorder that begin as an irritant dermatitis may progress to a localized Allergic or Atopic Dermatitis when reapplied. Because of release of vasoactive compounds from the immune cells, severe reactions can result in airway obstruction, hypotension, and cardiorespiratory arrest. The Food, Drug, and Cosmetics Act should be enforced. The Fair Packing and Labeling Act should be modified to state ALL ingredients of a product are required to be label specified. By doing so, the consumer could have avoided exposure to previously identified allergens, thus minimizing a potentially life threatening event.

36 THE UTILITY OF ACETAMINOPHEN SCREENING IN UNSUSPECTED SUICIDE INGESTIONS.

Lucanie R, Chiang WK, Reilly R. *Hudson Valley Regional Poison Center, Sleepy Hollow, NY*

Background: Acetaminophen (APAP) is one of the most common medications taken in overdoses. Because of the lack of specific symptoms associated with initial APAP toxicity and the availability of a specific antidote. Potential unsuspected APAP toxicity is a significant concern in all suicide ingestions. Objective: To identify the likelihood of unsuspected APAP toxicity in suicide ingestions. Methods: We performed a retrospective study of all suicide ingestions without a history of APAP exposure reported to a poison control center over a 6 month period. History, symptoms, and APAP levels were reviewed to assess the incidence of unsuspected APAP ingestions. All ingestions with a history of potential APAP involvement were excluded. Results: A total of 471 cases were identified, 151 cases

had APAP levels requested but the results were not documented. Of the remaining 320 cases, 23 (7.1%) were found to have APAP levels > 10 ug/mL. Twelve patients were treated with *N*-acetylcysteine (NAC) in the hospital, 7 patients (2.2%) had potentially toxic levels based on the Rumack-Matthew nomogram. The other 5 patients had non-toxic or un-interpretable levels. Even if we assume the 151 cases of undocumented levels were all non-toxic, the overall incidence of APAP toxicity is 1.5%. Conclusion: The risk of unsuspected acetaminophen toxicity is small but definite. Continued universal APAP screening in all suicide ingestions may be warranted. The use of NAC therapy in the hospitals often deviated from standard recommendations.

37 OBSERVATIONAL STUDY OF ACETAMINOPHEN OVERDOSE.

Rosen PB, Roth B, Woo O, Fernandez M, Chanez J, Shum S, Olson K. *Scott & White, Texas A & M, Temple, TX; California Poison Control System - San Francisco and Davis Division, University of California, San Francisco, CA; Central Texas, South Texas and Panhandle Poison Center, of the Texas Poison Center Network, San Antonio, TX*

Objective: To evaluate whether elevated AST, early in the clinical course of patients following acute acetaminophen (APAP) overdose might predict which patients might not need prolonged therapy with oral *N*-acetylcysteine (NAC). Background: Prior to the availability of an antidote, as many as 60% of patients, following an acute overdose, developed liver damage defined historically as aspartate aminotransferase (AST) greater than 1000 IU/L. Studies have documented the efficacy of a 72 hour course of oral NAC following acute ingestion of APAP. Those that do not have evidence of injury by 36 hours may do as well with a shorter course of NAC. Methods: This was a prospective observational study evaluating patients with toxic APAP blood levels, according to the Rumack-Matthew nomogram, following acute overdose. Five regional poison centers participated. Therapy with NAC was recommended for patients with continued elevation of AST four times the upper limit of normal past 36 hours. Otherwise, duration of therapy was determined by the treating physician. Results: Data was collected on 338 patients. 60 cases were excluded due to unknown time of ingestion, non-toxic APAP level, or insufficient AST measurements. There were 193 cases with AST under 4 times the upper limit of normal at 36 hours. 62 of these received no further NAC; None of these developed AST > 1000. 131 received further treatment, 2 (1.5%) developed AST > 1000. None developed liver failure. Conclusions: We found that following acute ingestion of toxic amounts of APAP, patients treated with NAC, rarely develop liver injury, as defined historically by AST > 1000, if the AST remained less than 4 times the upper limit of normal up to 36 hours post ingestion. These patients did well regardless of continued therapy with NAC.

38 DISPOSITION OF ACETAMINOPHEN OVERDOSE PATIENTS BY EMERGENCY PHYSICIANS.

Harris C, Engebretsen K. *Emergency Medicine Department, Regions Hospital, St. Paul, MN; International Poison Center, Bloomington, MN*

Objective: There are wide variations in the Emergency Department (ED) disposition of patients with acetaminophen (APAP) overdose, from ICU admission to treating the patient at home with the antidote, *N*-acetylcysteine (NAC). It is widely known that the early treatment with the antidote is very effective, and mortality from APAP overdose is low. The objective of this study was to evaluate the most common level of care involved in the hospital management of significant APAP overdose (requiring NAC therapy). Methods: This was a descriptive study design using a self-reporting survey instrument. A random sample of 1000 Emergency physicians (EPs) was obtained from the active member list of the American College of Emergency Physicians. A pilot survey was mailed to 50 randomly selected EPs from this list. After these were returned survey questions were reformatted or revised for clarification before mailing to the remaining 950 EPs. The survey requested information regarding hospital size, practice experience, and the typical disposition of acute APAP overdoses. A follow-up post card was sent to non-responders. Data from completed surveys was entered into a computer database for descriptive statistical analysis. Results: Of the 1000 surveys mailed, 591 were returned for a response rate of 58%. The completion rate was 57% (565). Over 2/3 (67.6%) of the responders of the total responders admitted their patients to the ICU. Only 19.4% admitted patients to the Step-down unit, and 12.6% to a ward bed. Nearly ninety percent (88.8%) are able to administer NAC in the ED. Conclusions: Two-thirds of EPs admit patients with significant APAP overdose to critical care bed in spite of the availability of an effective antidote and low mortality. Are critical care beds needed for APAP overdoses requiring NAC therapy? Further study is required to determine a safe and cost effective admit level.

39 ACETAMINOPHEN HEPATOTOXICITY AFTER CHRONIC RECTAL DOSING.

Robertson MA, Al-Binali A, Johnson DW. *Alberta Poison and Drug Information Service, Department of Pediatrics, University of Calgary, Calgary, Alberta, Canada*

Background: Recent pharmacokinetic studies in children administered a single dose of acetaminophen per rectum have suggested that up to 40 mg/kg/dose is required to achieve adequate serum concentration (Anesthesiology 1997;87:244). Some health care workers have extrapolated from these single-dose studies to recommend higher doses with chronic rectal administration. We report a case of a child we believe developed acetaminophen hepatotoxicity after his parents were instructed to administer per rectum 15-20 mg/kg every 3-4 hours. Case Report: An 8-year-old boy with congenital muscular dystrophy underwent a bilateral orchidopexy under regional anaesthesia. Following surgery and continuing after discharge, he was administered acetaminophen suppositories (17 mg/kg) every 3 hours for 60 hours (115 mg/kg/d). He was well for 24 hours, then developed anorexia, lethargy and vomiting. His parents sought medical care when they found him responsive only to pain. He was afebrile and his serum glucose was 1.0 mM. With glucose and fluid resuscitation he became lucid, but remained lethargic. He was noted to have tender hepatomegaly and ALT of 7777 IU/L, AST 7450 IU/L, PT 26.8 sec (INR 2.71), albumin 28 g/L, with normal NH_4 and bilirubin. He was treated with intravenous *N*-acetylcysteine for 60 hours with rapid improvement in liver function, appetite and mental status. On follow-up, 4 weeks later, ALT was 80 IU/L and all other liver function tests were normal. The clinical course and very high AST are most consistent with acetaminophen hepatotoxicity. Investigations were negative for an alternative toxic, viral or metabolic etiology for his liver dysfunction. Conclusion: This case suggests that the therapeutic index for chronic rectal dosing of acetaminophen is potentially as low as with oral administration. Health care workers should not extrapolate from pharmacokinetic studies of single-dose rectal administration of acetaminophen to make recommendations regarding chronic dosing per rectum that exceed 15 mg/kg/dose every 4 hours.

→ **40 INHERITED METABOLIC DISEASE MASQUERADING AS CHRONIC ACETAMINOPHEN TOXICITY.**

Lavalette JH, Tucker JR, Wiley JF II. *Connecticut Children's Medical Center, Hartford, CT; University of Connecticut School of Medicine, Farmington, CT*

Background: There have been recent concerns about chronic acetaminophen toxicity in pedatrics. Acetaminophen-induced hepatotoxicity should be considered early in the differential diagnosis of fulminant hepatic failure (FHF) so that antidotal treatment can be initiated. A case of FHF is presented in which initial investigations supported a possible diagnosis of acetaminophen toxicity, but the eventual etiology was a rare inherited metabolic disease. Case Report: A previously well 11-month-old male presented unresponsive with profound hypoglycemia after a 3-day illness of fever, vomiting, stomatitis and decreased intake. Recent medications included acetaminophen as suspension, suppositories, and as part of a multi-symptom cold remedy. In the emergency department, he was treated with IV dextrose with an excellent response, evaluated for presumed sepsis and started on antibiotics. He was maintained on dextrose containing IV fluid and on the morning after admission, he became unresponsive, requiring intubation. Significant laboratory studies at that time revealed a normal blood glucose, AST, ALT >10,000U/L, LDH-6180U/L, NH_3-190mcmol N/L/, PT >50sec, PTT-55sec, bilirubin-9.2/6.1mg/dL. He fulfilled the criteria for stage IV hepatic encephalopathy and was treated with aggressive supportive therapy including a double volume exchange transfusion. He was placed at the top of the liver transplant list. Multiple studies looking for infectious, toxic, and metabolic causes were performed. An acetaminophen level was 10mg/L. The last known dose of acetaminophen was prior to admission, more than 24 hours previously. Based on the exposure history and this clinical presentation, *N*-acetylcysteine therapy was initiated and continued for a full 72-hour course. He progressed to a full recovery and was discharged 10 days after admission. After discharge, metabolic studies revealed the etiology to be Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase (LCHAD) Deficiency. Conclusion: LCHAD deficiency is an extremely rare disorder of fatty acid oxidation that presents as episodes of acute illness triggered by prolonged fasting. In the future, the use of specific markers for acetaminophen-induced hepatotoxicity may help to separate acetaminophen-induced hepatic failure from other causes of FHF.

41 DO WE ADMINISTER *N*-ACETYLCYSTEINE (NAC) ON TIME? ADMISSION TO INPATIENT UNITS IS ASSOCIATED WITH DELAY IN NAC ADMINISTRATION.

Barton N, Wax PM, Cobaugh DJ. *Finger Lakes Regional Poison & Drug Information Center/University of Rochester, Rochester, NY*

Background: The objective of this study was to determine whether admission to the hospital floor after receiving a 1st dose NAC in the ED was associated with delayed administration of subsequent doses. Methods: We reviewed hospital records for all APAP overdoses presenting to a university hospital over 2 years who had a toxic APAP level and were admitted for NAC therapy. Information obtained included: time of ingestion, time of first three NAC doses,

location of NAC administration, and peak AST level during hospitalization. Results: Ninety-eight ... were reviewed. Sixteen were excluded because of incomplete data. Forty-three percent (35/82) of patients received their first NAC dose within 8 hours of APAP ingestion. Of the 82 cases that were analyzed, mean time between first and second NAC dose was 4.7 hours (SD 1.9) with median interval of 4 hours and range of 45 minutes to 12 hours. Time interval between doses was ≥ 6 h in 23% (19/82) of cases. 41% (34/82) received the 2nd NAC dose in the ED. Fifty-nine percent (48/82) received the 2nd NAC dose on the floor. Mean time between 1st and 2nd NAC was 5.1 h (SD 2.2) for patients transferred to the floor and 4.1 h (SD 1.0) for ED patients. In 2 patients who were transferred to a second hospital after the 1st NAC dose, time between 1st NAC dose and 2nd NAC dose was 8.5 and 12 hours. Of the 35 patients who received their first dose of NAC within 8 hours of ingestion, mean AST was 51 IU/L (SD 71) for those who received their 2nd NAC on the floor, and 29 IU/L (SD 12) for those who received their 2nd NAC in the ED. Conclusions: Timely administration of the second NAC dose may be delayed upon patient transfer from the ED to the floor. Delay is particularly problematic with inter-hospital transfers.

42 IMMEDIATE HYPERSENSITIVITY RELATED TO ORAL *N*-ACETYLCYSTEINE ADMINISTRATION FOR ACETAMINOPHEN TOXICITY.

Gomez M, Craft J, Shih RD, Marcus SM. *Morristown Memorial Hospital and The New Jersey Poison Center, Newark, NJ*

Background: The administration of *N*-acetylcysteine (NAC) is the treatment of choice for acetaminophen (APAP) poisoning. Allergic reactions have been associated with IV administration of NAC. However, immediate IgE mediated hypersensitivity reactions have not been well substantiated with orally administered NAC. We report such a case in the setting of acute APAP toxicity. Case Report: A 15-year-old female ingested 10 g APAP 6 hours prior to ED presentation. Her 6 hour post ingestion APAP level was 562 mcg/mL. Her first dose of NAC was administered 8 hours after ingestion followed by additional doses every 4 hours. Following the 6th NAC dose, she developed an urticarial rash over both forearms associated with pruritis. There were no associated respiratory or vital sign abnormalities at this time. She received diphenhydramine (DPH) with resolution of her rash. Following subsequent NAC doses she had recurrent urticaria and pruritis with the development of swelling, erythema and tenderness of the plantar aspect of her right foot. She was managed successfully with DPH, methylprednisolone and discontinuation of the NAC after the 11th dose. Serum IgE after the last NAC dose was elevated at 624 u/mL. A CBC at that time was normal with no eosinophilia. Conclusion: A case of IgE mediated immediate hypersensitivity is presented associated with the oral administration of *N*-acetylcysteine for acetaminophen toxicity.

43 DOES ORAL *N*-ACETYLCYSTEINE REDUCE THE ADSORPTION OF ACETAMINOPHEN BY ACTIVATED CHARCOAL?

Tenenbein PK, Sitar DS, Tenenbein M. *University of Manitoba, Winnipeg, Manitoba, Canada*

Background: Whether concomitant oral administration of *N*-acetylcysteine and activated charcoal reduces the bioavailability of *N*-acetylcysteine has been studied many times. This study tests the hypothesis that concomitant administration reduces the adsorptive capacity of charcoal for acetaminophen. Methods: This was an *in vitro* study. Reagents included were the pharmaceutical preparation of *N*-acetylcysteine, powdered acetaminophen and powdered activated charcoal. Acetaminophen analyses were by HPLC and all measurements were done in triplicate or greater. All experiments were performed at pH 1.8 and 7.4 and *N*-acetylcysteine was added after the incubation of acetaminophen and charcoal. Percent binding of acetaminophen was calculated after its incubation with charcoal both with and without the addition of *N*-acetylcysteine over a range of clinically relevant charcoal to acetaminophen ratios. To further test the hypothesis the latter experiment was repeated with increasing amounts of *N*-acetylcysteine to provide this antidote with a competitive advantage for charcoal binding sites. Data were compared using the unpaired two-sided student t-test. A difference was accepted when $p<0.05$. Results: Differences between control and experimental data were similar at both pH values. At pH 7.4 the addition of *N*-acetylcysteine altered the binding of acetaminophen by activated charcoal from 90.6% to 89.6% ($p=0.005$) and from 98.5% to 98.6% ($p=1.0$) at activated charcoal to acetaminophen ratios of 5:1 and 10:1 respectively. Although the first comparison is significant it is likely clinically unimportant as a 1% difference equals 100 mg of acetaminophen when 10.0 g are ingested. Increasing the amount of *N*-acetylcysteine decreased the amount of bound acetaminophen from 98.5% to 82%. Conclusions: The hypothesis is supported. Concomitant oral administration of activated charcoal and *N*-acetylcysteine reduces the adsorptive capacity of charcoal for acetaminophen. The extent is likely clinically unimportant for mild to moderate acetaminophen ingestions. However, it becomes important in situations of diminished charcoal to ingestant ratios (< 5.0:1) such as massive acetaminophen overdose or the presence of coingestants. Intravenous administration of *N*-acetylcysteine circumvents this interaction.

Platform Session 3 — Sunday, September 13 — 4:00 pm – 5:00 pm
Treatment Protocols
Abstracts #117–#120

117 CHRONIC ETHANOL USE AND ACUTE ACETAMINOPHEN OVERDOSE TOXICITY.

Smilkstein MJ, Rumack BH. *Rocky Mountain Poison Center, Denver, CO; Oregon Poison Center, Portland, OR*

Objective: To compare acute acetaminophen overdose hepatotoxicity in patients with and without chronic ethanol use. Methods: Cases from the National Multicenter Study of Oral *N*-acetylcysteine meeting the following criteria were included: acute acetaminophen overdose, age >10 years, completed *N*-acetylcysteine treatment, valid plasma acetaminophen concentration ([APAP]), and adequate aminotransferase data. If chronic ethanol abuse or alcoholism was noted, cases were considered ethanol$_c$(+). If ethanol use was negative, acute only, or not documented, cases were considered ethanol$_c$(-). Maximum recorded AST, and the proportion of cases with AST or ALT >1000 IU/L were compared between ethanol$_c$(+) and ethanol$_c$(-) cases overall, as well as within subgroups defined by [APAP] risk stratification, time to first *N*-acetylcysteine dose or both. Statistics included t-test of independent samples (means), Kruskal-Wallis 1-way Anova (medians), and Chi-square (proportions). Results: 115 ethanol$_c$(+) and 2321 ethanol$_c$(-) cases were included. As a group, ethanol$_c$(+) cases were older and more often male, but no different in APAP dose by history, [APAP] risk stratification, or time to first *N*-acetylcysteine. Overall, ethanol$_c$(+) cases had higher mean AST(1647±322 vs 608±38 IU/L, p=.002), median AST(49 vs 38 IU/L, p=.013) and proportion with AST or ALT>1000 IU/L(26% vs 13%, p=.0001). The same was true within traditional at-risk subgroups (e.g., "possible", "probable", "high" risk) defined by [APAP]; and among all cases first receiving *N*-acetylcysteine after >8 hours (N=1730). Among cases traditionally considered at low risk ([APAP] below the "200/probable risk" line (N=1014), or *N*-acetylcysteine started within 8 hours (N=706)), there was no difference in any outcome variable between ethanol$_c$ groups. By multiple linear regression, the ethanol-AST association remained significant (p=.0001) after effects of age, gender, time to *N*-acetylcysteine, and [APAP] risk group were considered. Conclusions: Acute acetaminophen overdose with chronic ethanol use was associated with increased hepatotoxicity among at-risk cases. Chronic ethanol use did not increase hepatotoxicity among low risk cases, suggesting that changes in *N*-acetylcysteine initiation guidelines on the basis of chronic ethanol use are unwarranted.

118 VALIDATION OF A SHORTER TREATMENT PROTOCOL FOR ACUTE ACETAMINOPHEN POISONING BASED ON EVIDENCE OF LIVER INJURY.

Roth B, Woo O, Olson K, Albertson T, Geller R, Clark R. *California Poison Control System, University of California San Francisco, San Francisco, CA*

Background: The 72 hour treatment regimen for acetaminophen poisoning is based on an uncontrolled, open study performed for the purposes of showing efficacy and safety to gain FDA approval. The decision to utilize a 72 hour regimen in the original protocol was not based on experimental data (e.g., biokinetic monitoring). A prospective observational study was undertaken to test the hypothesis that patients with normal AST and ALT levels determined 36 hours after acetaminophen overdose do not subsequently develop hepatic injury with N-acetyl cysteine (NAC) is discontinued. Methods: If AST and ALT were normal 36 hours after the ingestion, poison control center (PCC) recommendations were that NAC be discontinued. If AST and ALT were abnormal it was recommended that therapy with NAC be continued until normalization of liver function studies or until the patient received 72 hours of therapy. Data was collected prospectively in the course of usual telephone consults provided by the Poison Control System. Results: 250 consecutive patients were evaluated. 60% of patients had normal AST and ALT 36 hours from the time of ingestion. All of these patients did well without subsequently developing biochemical or physical evidence of liver injury. Of the 149 patients with normal AST and ALT at 36 hours 102 were treated for an average of 16 hours longer than PCC recommendations; 31 were treated for an average of 5 hours less than PCC recommendations; 16 were treated exactly as recommended. Despite inexact adherence to PCC recommendations average duration of therapy with NAC for this group was 36 hours. Follow up was obtained in 90% of cases. Conclusions: Patients without biochemical evidence of liver injury 36 hours after acute acetaminophen overdose require no further therapy with NAC.

119 GASTRIC LAVAGE FOR LIQUID POISONS.

Grierson R, Green R, Sitar DS, Tenenbein M. *University of Manitoba, Winnipeg, Manitoba, Canada*

Background: Although gastric lavage is no longer considered as routine therapy for the overdose patient, there are